

Amendments to the Claims:

Please cancel claims 1-31 and 58-71 without prejudice.

The following listing of claims replaces any prior versions.

Please amend the claims noted as "Currently Amended".

Listing of Claims:

The listing of claims will replace all prior version, and listings, of claims in the application:

Claims 1-31 (Canceled)

32. (Currently Amended): A method of screening for identifying an agent that affects isopeptidase activity of a polypeptide comprising a JAM domain, wherein the isopeptidase activity ~~deconjugation of~~ deconjugates a modifier protein from a target protein, wherein the modifier protein is conjugated to the target protein via a peptide bond between the carboxy terminus of the modifier protein and a free amino group of the target protein, the method comprising:

~~incubating in the presence and absence of a test agent, the target protein and polypeptide comprising a JAM domain consisting essentially of an amino acid sequence of HXHXXXXXXXXXXD, wherein H is histidine, D is aspartate, and X is any amino acid,~~

~~determining the effect of the test agent, the isopeptidase activity of the polypeptide in the presence and absence of the test agent, wherein an increase or decrease a difference in the amount of the target protein not conjugated to the modifier protein caused by isopeptidase activity in the presence versus the absence of the test agent is indicative of an agent affecting that affects deconjugation of the modifier protein from the target protein isopeptidase activity of the polypeptide.~~

33. (Original): The method of claim 32, wherein the JAM domain consists essentially of an amino acid sequence of GW(Y/I)H(S/T)HPXXXXXXXXSXXD (SEQ ID NO. 2), wherein G is glycine, W is tryptophan, Y is tyrosine, I is isoleucine, H is histidine, S is serine, T is threonine, P is proline, D is aspartate, X is any amino acid, Y/I is either Y or I, and S/T is either S or T.
34. (Original): The method of claim 32, wherein the target protein is a cullin protein
35. (Original): The method of claim 34, wherein the target protein is Cul1, Cul2, Cul3, Cul4A, Cul4B, or Cul5.
36. (Original): The method of claim 32, wherein the target protein has ubiquitin ligase activity.
37. (Original): The method of claim 32, wherein the target protein is part of a protein complex having ubiquitin ligase activity.
38. (Original): The method of claim 32, wherein the modifier protein is NEDD8, UBL1, SMT3H2, SMT3H1, APG12, FAT10, Fau, UCRP, URM1, or UBL5.
39. (Original): The method of claim 32, wherein the polypeptide is a polypeptide complex of COP9/signalsome.
40. (Original): The method of claim 32, wherein the polypeptide is AMSH, AMSH1, or AMSH2.

41. (Original): The method of claim 32, wherein a test agent decreasing the amount of the target protein not conjugated to the modifier protein is indicative of an agent decreasing deconjugation of the modifier protein from the target protein.
42. (Original): The method of claim 32, wherein the target protein has the activity of peroxidase, alkaline phosphatase, or luciferase.
43. (Original): The method of claim 32, wherein the target protein is a fluorescent protein.
44. (Original): The method of claim 43, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein, yellow fluorescent protein, cyan fluorescent protein and dsRed.
45. (Original): The method of claim 43, wherein the target protein is a fluorescent protein via chemical modification.
46. (Original): The method of claim 32, wherein the target protein causes production of a detectable signal upon deconjugation from the modifier protein.
47. (Original): The method of claim 32, wherein the polypeptide is a polypeptide complex of 26S proteasome.
48. (Original): The method of claim 32, wherein the polypeptide is a polypeptide complex of 26S proteasome and the modifier protein is an ubiquitin.
49. (Original): The method of claim 47, wherein the incubation is conducted in the presence and absence of the test agent, the target protein, the 26S proteasome, and a 20S inhibitor.

50. (Original): The method of claim 47, wherein the incubation is conducted in the presence and absence of the test agent, the target protein, the 26S proteasome, a 20S inhibitor, and ATP.
51. (Original): The method of claim 50, wherein the incubation further includes an inhibitor of deubiquitination by an ubiquitin isopeptidase.
52. (Original): The method of claim 47, wherein the target protein not conjugated to the modifier protein is not degraded.
53. (Original): The method of claim 47, wherein the target protein is Sic1.
54. (Original): The method of claim 47, wherein the 26S proteasome is purified from *S. cerevisiae*.
55. (Original): The method of claim 47, wherein the 26S proteasome is purified from eukaryotic cells.
56. (Original): The method of claim 47, wherein the 26S proteasome is purified from human cells.
57. (Original): The method of claim 32, wherein the test agent is a member of a compound library selected from the group consisting of hydroxamate compound library, reverse hydroxamate compound library, carboxylate compound library, thiol compound library, and phosphonate compound library.

Claims 58-71 (Canceled)

72. (New): The method of claim 32, wherein the polypeptide comprising the JAM domain comprises Rpn11.

73. (New): The method of claim 72, wherein the polypeptide comprising the JAM domain is Rpn11.

74. (New): The method of claim 72, wherein the method further comprises carrying out the incubation in the presence of an inhibitor of degradation of the target.

75. (New): The method of claim 32, further comprising after the incubation, determining whether the modifier protein remains conjugated to the target protein via a peptide bond between the carboxy terminus of the modifier protein and a free amino group of the target protein.

76. (New): The method of claim 32, wherein the polypeptide comprising the JAM domain has isopeptidase activity.